REMARKS

Applicants have amended claims 1 and 24 to delete the recitation of mumps virus, measles virus, and metapneumovirus. The amendment introduces no new matter.

Upon entry of these amendments, claims 1, 3, 5, 6, 8, 11, 13, 18, 22-25, 30, 33, 35, 37, 41-43, 46, 48-50, 54, 55, 60-63, 86, 105, and 122-124 will be pending in the application. Of these, claims 43, 46, 48-50, 54, 55, 60-63, 86, 105, and 122-124 are withdrawn.

REJECTIONS TO THE CLAIMS

Claim Rejection under 35 U.S.C. § 112, First Paragraph

Claims 1, 3, 5, 6, 8, 11, 13, 22-25, 30, 33, 35, 37, 41, and 42 stand rejected under 35 U.S.C. § 112, first paragraph, allegedly for failing to comply with the written description requirement. Specifically, the Examiner contends that Tannock GA et al., Journal of Clinical Microbiology 25:1769-1771 (1987) ("Tannock") "teaches" that different strains of RSV have different stability after freeze drying. The Examiner further contends that the specification "fails to provide adequate teaching under the quid pro quo doctrine", and that applicants' teaching is not commensurate with the scope of the claims. For the sole purpose of expediting the allowance of the application, Applicants have amended claims 1 and 24. Former claims 1 and 24 each recite five types of viruses (RSV, PIV, mumps virus, measles virus, or metapneumovirus), or a combination thereof. Claims 1 and 24 have been amended to recite only respiratory syncytial virus, parainfluenza virus, and a combination thereof. Working examples in the application as filed demonstrate the production of storage stable compositions involving RSV and PIV using the claimed methods. Applicants respectfully submit that the disclosure of the specification reasonably conveys to a person skilled in the art that the inventors had possession of the claimed invention at the time the application was filed and, accordingly, the rejection is overcome.

Claim Rejection under 35 U.S.C. § 102(b)

Claims 1, 3, 5, and 6 stand rejected as allegedly anticipated by Tannock. These claims are drawn to a process of producing a storage stable virus composition. In the previous Office Action, the Examiner asserts that the Patent Office lacks the facilities to

perform comparisons between the claimed materials and prior art materials that reasonably appear to meet the claim limitations and therefore the burden is properly shifted to applicant to distinguish the claimed product from the prior art product. In the present Office Action, the Examiner specifically alleges that "the virus used, the buffer used, the step of free drying used and stability of the product of the method appear to be the same in the prior art as claimed" and consequently maintains that the burden is on the Applicants to differentiate the methods. Applicants respectfully traverse.

Applicants submit that, contrary to the Examiner's assertion that the methods appear to be the same, there are substantial differences between the claimed methods and the disclosure of Tannock, First, Applicants submit that the buffer used in the claimed invention is different from the one disclosed in Tannock. Tannock prepared the virus formulation in SPGA that includes sucrose, sodium glutamate, and bovine albumin (See column 2, paragraph 2 of Tannock). Tannock specifically teaches that sucrose is the essential component of SPGA for preserving the structure and/or infectivity of various viruses. None of these components is recited in any of the rejected claims. Specifically, claim 6, the only rejected claim that recites a buffer, recites that the virus composition is formulated in a 5.0 mM to about 20 mM phosphate buffer solution comprising sodium and/or potassium monobasic and dibasic salts and having a pH of about 6.5 to about 7.8.

Applicants further submit that the steps of freeze drying used are also different. For example, claim 1, as amended, as well as claims 3, 5 and 6 by dependency, recite freezing a virus composition "below its glass transition temperature in a time of 60 minutes or less at a rate of -0.5°C to -2.5°C per minute." Claim 3, which depends from claim 1, recites the additional element "wherein the glass transition temperature is about -30°C to about -50°C." Claim 5, which depends from claim 3, further recites "wherein the glass transition temperature of about -35°C is reached in a time of 20 minutes or less." Tannock does not disclose "glass transition temperature," nor the time to reach such temperature, nor a freezing rate of "-0.5°C to -2.5°C per minute." The Examiner also concedes that Tannock is silent on these limitations.

Moreover, Applicants submit that stability of the product is different as well. Claim 1 recites that "the lyophilized virus composition has less than about a 17.6% log PFU loss after at least one year at a storage temperature of about 1°C to about 10°C as compared to the lyophilized virus composition before storage." The Examiner points to Table 2 in Tannock as disclosing the stability of the Tannock product. However, contrary to the Examiners' assertion, the data in Table 2 suggest that the Tannock products have more than 17.6% log PFU loss after storage temperature of 4°C for only 45 weeks. Specifically, Table 2 provides stability data for the freeze dried product of three RSV strains (11657, R-5059, and M-1016) held at -80 °C, -20 °C, 4 °C, 25 °C, and 37 °C for up to 45 weeks. These products have an initial titer of $10^{5.9}$ to $10^{6.3}$ PFU per ampoule. After storage for 45 weeks at 4 °C, which is the only example in Tannock within the temperature range recited in claim 1, the titer of strain 11657 lost at least 18% (from Log_{10} 5.9 - 6.3 down to 4.83) and the titer of strain R-5059 lost at least 49% (from Log_{10} 5.9 – 6.3 down to 3.04). While the measured titer for the third strain, M-1016, at 45 weeks was higher than the initial titer, according to the author this has to do with assay variations and disaggregation of clumped particles after reconstitution of the freeze-dried material and, therefore, it does not accurately reflect the stability of the product (See page 1771, left hand column). Accordingly, Tannock does not teach the stability recited in the claims of the present application.

For at least the above reasons, Tannock does not disclose all the limitations of the claims and consequently it does not anticipate the claimed invention.

Claim Rejection under 35 U.S.C. § 103(a)

Claims 1, 3, 5, 6, 8, 11, 18, 22-25, 30, 33, 35, 41, and 42 stand rejected as allegedly being obvious over Tannock and Parrington M et al., International Application Publication No. WO02/09749 ("Parrington"). In particular, the Examiner asserts that Tannock "teaches" a 0.5 ml stabilized freeze dried RSV sample in SPGA buffer using a commercial freeze-drying system, wherein the freeze-drying is done under vacuum, nitrogen is added to the chambers, and the ampoule is sealed. The Examiner concedes that Tannock does not teach a variety of buffers or freeze-drying conditions. The

Examiner points to Parrington's alleged recitation of buffers and a freezing rate of -2°C per minute to remedy this defect. Applicants traverse.

In response to the rejection in the previous Office action, Applicants argued that there would have been no motivation to modify a method for freeze-drying a virus with steps for freeze drying a protein, nor would there have been any reasonable expectation of success even if one were motivated to do so because Parrington is directed to freeze-dried compositions of RSV proteins, not to freeze-dried compositions of an RSV virus. Applicants explained that Paramyxoviruses are composed of RNA and a number of different proteins packaged in a viral envelope and, therefore, one would appreciate that viruses are significantly more complex than isolated proteins and would not expect methods for freezing protein to be applicable to the virus. In response to the Applicants' arguments, the Examiner responded in this Office Action that "protein needs to be stabilized to stabilize the virus" and that "degraded proteins would mean degraded virions as well." (See page 5). While the Examiners' above assertions might be correct, the converse is not necessarily so. According to Tannock and as recognized by the Examiner, RSV is extremely susceptible to loss of potency after freezing and thawing. As is known in the art a virus is a complex living organism, which, as the Examiner recognizes, is composed of a genomic segment in addition to proteins. If other components or structure, such as the genomic segment, is degraded the potency of a virus is expected to be affected even if the proteins are stabilized. Based on the disclosure of Tannock and Parrington and what is known in the art, a person skilled in the art would believe that it takes a lot more to stabilize a complex living virus than just the protein components and would have no reason to believe that merely stabilizing one or more proteins of the virus would stabilize the virus as a living organism. Accordingly, Applicants maintain that there would have been no motivation to combine the teaching of Tannock and Parrington, nor would there have been any reasonable expectation of success even if one were motivated to do so.

Claims 13 and 37 stand rejected as allegedly obvious over Tannock and Parrington, and further in view of Suzuki M, Journal of Hygiene 68, 29-41 (1970) ("Suzuki").

Claim 13, which depends from claim 11, incorporates the limitations of claims 1, 6, 8, and 11 and further recites soy peptone. Similarly, claims 37, which depends from claim 35 and incorporates the limitations of claims 24, 25, 30, 33, and 35, further recite soy peptone. The Examiner relies on Suzuki to "teach" that peptone stabilizes freeze-dried smallpox and concludes that it would have been obvious to one of skill in the art to use soy peptone in the alleged method of Tannock and Parrington for stabilizing a freeze-dried virus. Applicants traverse.

As described above, the Examiner's combination of Tannock and Parrington fails to render the pending claims obvious. Any alleged recitation of peptone or soy peptone in Suzuki does not remedy this defect.

For at least the above reasons, Applicants respectfully request that the Examiner withdraw the obviousness rejection.

CONCLUSION

In view of the foregoing amendments, evidence, and arguments, Applicants respectfully submit that claims 1, 3, 5, 6, 8, 11, 13, 18, 22-25, 30, 33, 35, 37, 41-43, 46, 48-50, 54, 55, 60-63, 86, 105, and 122-124 are in condition for allowance. A Notice of Allowance is respectfully requested.

Respectfully submitted,

Date: June 3, 2011

/Austin W. Zhang/
Austin W. Zhang
Attorney For Applicants
Registration No. 48,061

Pfizer Inc
Legal Division – Intellectual Property
10555 Science Center Drive
San Diego, California 92121
Phone: (858) 622-7950
Fax: (858) 678-8233
austin.w.zhang@pfizer.com